International Appl. No. PCT/CA2004/000033

**United States National Phase Entry** 

Amdt. Dated June 14, 2006

## **Amendments to the Claims:**

Please number the claim pages to begin at page 100.

This listing of claims will replace all prior versions, and listings, of claims in the application.

## **Listing of Claims:**

1 - 46 (Cancelled).

47. (New) An array comprising two or more nucleic acid molecules immobilized on a substrate, wherein the two or more nucleic acid molecules each comprise a sequence that hybridizes to one ATP-binding cassette (ABC) transporter gene.

48. (New) The array according to claim 47, wherein the two or more nucleic acid molecules each comprise a portion of the 3' untranslated region of the ABC transporter gene.

49. (New) The array according to claim 47, wherein the two or more nucleic acid molecules each comprise a nucleic acid sequence selected from:

- (a) the nucleic acid sequences as shown in SEQ ID NOS: 1 to 47 and Figures 1 to 47, wherein T can also be U;
- (b) nucleic acid sequences complementary to (a);
- (c) nucleic acid sequences which are homologous to (a) or (b); or
- (d) a fragment of (a) to (c), which comprises a sequence that hybridizes to one of the ABC transporter genes.
- 50. (New) The array according to claim 47, wherein the array is a microarray.
- 51. (New) A method of detecting the expression of two or more ATP-binding cassette (ABC) transporter genes, comprising the steps:
  - (a) providing two or more nucleic acid molecules, each comprising a sequence that hybridizes to one ABC transporter gene;
  - (b) providing transcription indicators from a test sample;

- (c) allowing the transcription indicators to hybridize with said two or more nucleic acid molecules; and
- (d) detecting hybridization of said transcription indicators with said two or more nucleic acid molecules.

wherein hybridization is indicative of the expression of the ABC transporter genes.

- 52. (New) The method according to claim 51, wherein the two or more nucleic acid molecules each comprise a portion of the 3' untranslated region of the ABC transporter gene.
- 53. (New) The method according to claim 51, wherein the two or more nucleic acid molecules each comprise a nucleic acid sequence selected from:
  - (a) the nucleic acid sequences as shown in SEQ ID NOS: 1 to 47 and Figures 1 to 47, wherein T can also be U:
  - (b) nucleic acid sequences complementary to (a);
  - (c) nucleic acid sequences which are homologous to (a) or (b); or
  - (d) a fragment of (a) to (c), which comprises a sequence that hybridizes to one of the ABC transporter genes.
- 54. (New) The method according to claim 51, wherein the two or more nucleic acid molecules that each comprise a sequence that hybridizes to one ABC transporter gene, are prepared using PCR and primer pairs, wherein the primer pairs comprise a nucleic acid sequence selected from one or more of the group comprising:
  - (a) one or more isolated and purified pairs of nucleic acid sequences selected from:

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SEQ ID NO: 48 and SEQ ID NO: 49;
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SEQ ID NO: 50 and SEQ ID NO: 51;

SEQ ID NO: 52 and SEQ ID NO: 53;

SEQ ID NO: 54 and SEQ ID NO: 55;

SEQ ID NO: 56 and SEQ ID NO: 57;

SEQ ID NO: 58 and SEQ ID NO: 59;

SEQ ID NO: 60 and SEQ ID NO: 61;

SEQ ID NO: 62 and SEQ ID NO: 63;

SEQ ID NO: 64 and SEQ ID NO: 65;

SEQ ID NO: 66 and SEQ ID NO: 67;

SEQ ID NO: 68 and SEQ ID NO: 69; SEQ ID NO: 70 and SEQ ID NO: 71: SEQ ID NO: 72 and SEQ ID NO: 73; SEQ ID NO: 74 and SEQ ID NO: 75; SEQ ID NO: 76 and SEQ ID NO: 77; SEQ ID NO: 78 and SEQ ID NO: 79; SEQ ID NO: 80 and SEQ ID NO: 81; SEQ ID NO: 82 and SEQ ID NO: 83; SEQ ID NO: 84 and SEQ ID NO: 85; SEQ ID NO: 86 and SEQ ID NO: 87; SEQ ID NO: 88 and SEQ ID NO: 89: SEQ ID NO: 90 and SEQ ID NO: 91; SEQ ID NO: 92 and SEQ ID NO: 93; SEQ ID NO: 94 and SEQ ID NO: 95; SEQ ID NO: 96 and SEQ ID NO: 97; SEQ ID NO: 98 and SEQ ID NO: 99; SEQ ID NO: 100 and SEQ ID NO: 101; SEQ ID NO: 102 and SEQ ID NO: 103: SEQ ID NO: 104 and SEQ ID NO: 105; SEQ ID NO: 106 and SEQ ID NO: 107; SEQ ID NO: 108 and SEQ ID NO: 109; SEQ ID NO: 110 and SEQ ID NO: 111; SEQ ID NO: 112 and SEQ ID NO: 113: SEQ ID NO: 114 and SEQ ID NO: 115; SEQ ID NO: 116 and SEQ ID NO: 117; SEQ ID NO: 118 and SEQ ID NO: 119; SEQ ID NO: 120 and SEQ ID NO: 121; SEQ ID NO: 122 and SEQ ID NO: 123: SEQ ID NO: 124 and SEQ ID NO: 125; SEQ ID NO: 126 and SEQ ID NO: 127; SEQ ID NO: 128 and SEQ ID NO: 129; SEQ ID NO: 130 and SEQ ID NO: 131: SEQ ID NO: 132 and SEQ ID NO: 133;

SEQ ID NO: 134 and SEQ ID NO: 135;

SEQ ID NO: 136 and SEQ ID NO: 137;

SEQ ID NO: 138 and SEQ ID NO: 139; and

SEQ ID NO: 140 and SEQ ID NO: 141;

- (b) the nucleic acid sequences in (a) wherein T can also be U;
- (c) nucleic acid sequences complementary to (a) or (b); and
- (d) nucleic acid sequences which are homologous to (a), (b) or (c).
- 55. (New) The method according to claim 51 wherein the transcription indicators are selected from the group consisting of transcripts of the gene or genes, cDNA reverse transcribed from the transcript, cRNA transcribed from the cDNA, DNA amplified from the genes, and RNA transcribed from amplified DNA.
- 56. (New) The method according to claim 51 performed in microarray format.
- 57. (New) The method according to claim 51, further comprising the steps of:
  - (a) generating a set of expression data;
  - (b) storing the data in a database; and
  - (c) performing comparative analysis on the set of expression data, thereby analyzing ABC transporter gene expression.
- 58. (New) A method for screening compounds for their effect on the expression of one or more ATP-binding cassette (ABC) transporter genes comprising:
  - (a) exposing a test sample to one or more compounds;
  - (b) providing a transcription indicator from the test sample;
  - (c) providing one or more nucleic acid sequences, each comprising a sequence that hybridizes to one ABC transporter gene;
  - (d) allowing said transcription inhibitor to hybridize with said one or more nucleic acid sequences; and
  - (e) detecting hybridization of said transcription indicator with said one or more nucleic acid sequences,

wherein hybridization is indicative of expression of the one or more ABC transporter gene expression.

59. (New) The method according to claim 58 further comprising the step of quantitatively or qualitatively comparing the hybridization detected in step (e) with the hybridization of transcription indicators from a control sample, thereby determining the effect of the one or more compounds on the expression of the one or more ABC transporter genes.

- 60. (New) A method for screening compounds for their effect on the expression of one or more ATP-binding cassette (ABC) transporter genes comprising:
  - (a) preparing an ABC transporter gene expression profile, using a method according to claim 51, of a test sample that has been exposed to one or more compounds;
  - (b) preparing an ABC transporter gene expression profile, using a method according to claim 51, of a control sample; and
  - (c) quantitatively or qualitatively comparing the gene expression profiles from (a) and (b),

wherein differential expression profiles in (a) and (b) is indicative of a compound having an effect on the expression of one or more ABC transporter genes.

- 61. (New) The method according to claim 60, wherein if the expression of one or more of the ABC transporter genes in the test sample is increased compared to the control sample, then the efficacy of the one or more compounds may be decreased.
- 62. (New) The method according to claim 60, wherein if the expression of one or more of ABC B1 (MDR1), ABC C1 (MRP1), ABC C2 (MRP2), and ABC G2 (BCRP) in the test sample is increased compared to the control sample, then the efficacy of the one or more compounds may be decreased.
- 63. (New) The method according to claim 60, wherein if the expression of one or more of the ABC transporter genes in the test sample is decreased compared to the control sample, then the efficacy or toxicity of the one or more compounds may be increased.
- 64. (New) The method according to claim 60, wherein if the expression of one or more of ABC B1 (MDR1), ABC C1 (MRP1), ABC C2 (MRP2), and ABC G2 (BCRP) in the test sample is decreased compared to the control sample, then the efficacy and/or toxicity of the one or more compounds may be increased.

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65. (New) A method of assessing the toxicity and/or efficacy of a compound in a subject comprising:

- (a) preparing an ATP-binding cassette (ABC) transporter gene expression profile, using a method according to claim 51, of a test sample that has been exposed to the compound;
- (b) preparing an ABC transporter gene expression profile, using a method according to claim 51, of a control sample; and
- (c) quantitatively or qualitatively comparing the gene expression profiles from (a) and (b),

wherein a difference in the ABC transporter gene expression profiles in (a) and (b) is indicative of the toxicity and/or efficacy of the compound.

- 66. (New) A method for determining a change in ATP-binding cassette (ABC) transporter gene expression profile for a compound in the presence of one or more different compounds comprising:
  - (a) preparing an ABC transporter gene expression profile, using a method according to claim 51, of a test sample that has been exposed to the compound;
  - (b) preparing an ABC transporter gene expression profile, using a method according to claim 51, of a test sample that has been exposed to the compound and the one or more different compounds; and
- (c) quantitatively or qualitatively comparing the gene expression profile in (a) and (b), wherein differential expression in (a) and (b) indicates that the ABC transporter gene expression profile of the compound changes in the presence of the one or more different compounds.
- 67. (New) The method according to claim 66, wherein changes in the ABC transporter gene expression profile indicate the presence of drug-drug interactions.
- 68. (New) The method according to claim 58 wherein the hybridization is detected over a period of time at specified time intervals.
- 69. (New) A kit, comprising one or more of the following: a nucleic acid array according to claim 47, reagents for use with the arrays, signal detection and array-processing instruments,

gene expression databases or analysis and database management software.

- 70. (New) A relational database comprising ATP-binding cassette (ABC) transporter gene expression profiles obtained using the method according to claim 51.
- 71. (New) Two or more isolated nucleic acid molecules, wherein each of the nucleic acid molecules comprises a sequence that hybridizes to one ATP-binding cassette (ABC) transporter gene.
- 72. (New) The two or more isolated nucleic acid molecules according to claim 71, wherein each of the nucleic acid molecules comprise a portion of the 3' untranslated region of the ABC transporter gene.
- 73. (New) The two or more isolated nucleic acid molecules according to claim 71, wherein each of the nucleic acid molecules comprise a nucleic acid sequence selected from:
  - (a) the nucleic acid sequences as shown in SEQ ID NOS: 1 to 47 and Figures 1 to 47, wherein T can also be U;
  - (b) nucleic acid sequences complementary to (a);
  - (c) nucleic acid sequences which are homologous to (a) or (b); or
  - (d) a fragment of (a) to (c), which comprises a sequence that hybridizes to one of the ABC transporter genes.
- 74. (New) Two or more pairs of primers for preparing the two or more nucleic acid molecules according to claim 71.
- 75. (New) Two or more pairs of primers according to claim 74, wherein the primers comprise a nucleic acid sequence selected from the group consisting of:
  - (a) a nucleic acid sequence as shown in SEQ ID NOS: 48 to 141 and Table 1, wherein T can also be U;
  - (b) nucleic acid sequences complementary to (a); and
  - (c) nucleic acid sequences which are homologous to (a) or (b).
- 76. (New) Two or more pairs of primers, wherein the primer pairs comprise a nucleic acid

## sequence selected from one or more of:

(a) one or more isolated and purified pairs of nucleic acid sequences selected from:

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SEQ ID NO: 48 and SEQ ID NO: 49;
SEQ ID NO: 50 and SEQ ID NO: 51:
SEQ ID NO: 52 and SEQ ID NO: 53;
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SEQ ID NO: 60 and SEQ ID NO: 61;
SEQ ID NO: 62 and SEQ ID NO: 63;
SEQ ID NO: 64 and SEQ ID NO: 65;
SEQ ID NO: 66 and SEQ ID NO: 67;
SEQ ID NO: 68 and SEQ ID NO: 69:
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SEQ ID NO: 114 and SEQ ID NO: 115;
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SEQ ID NO: 128 and SEQ ID NO: 129;
SEQ ID NO: 130 and SEQ ID NO: 131;
SEQ ID NO: 132 and SEQ ID NO: 133;
SEQ ID NO: 134 and SEQ ID NO: 135;
SEQ ID NO: 136 and SEQ ID NO: 137;
SEQ ID NO: 138 and SEQ ID NO: 139; and
SEQ ID NO: 140 and SEQ ID NO: 141;
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- (b) the nucleic acid sequences in (a) wherein T can also be U;
- (c) nucleic acid sequences complementary to (a) or (b); and
- (d) nucleic acid sequences which are homologous to (a), (b) or (c).
- 77. (New) Isolated nucleic acid molecules prepared using PCR and the pairs of primers according to claim 76.